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Editorial

The role of post-translational protein modifications on heart and vascular metabolism

The emergence of metabolism as playing a crucial role in cardiovascular health has generated significant insights into cardiovascular disease development and potential new treatments. In order to provide a forum for the free exchange of ideas by investigators with a special interest in the multiple roles of intermediary metabolism in the cardiovascular system, in 2000 the Society for Heart and Vascular Metabolism (SHVM) was founded. Each year, the SHVM selects a theme for their annual meeting that focuses on some of the most recent research advances and emerging areas of importance in cardiovascular metabolism. The 2015 meeting, held in Tarrytown N.Y., U.S.A., focused on novel scientific discoveries that provide mechanistic insight into cardiac metabolic dysregulation with an emphasis on translational and post-translational protein modifications, amino acid metabolism and protein catabolism. Based on this, a special issue of review articles that highlight the importance of protein and amino acid metabolism and the role of post-translational protein modifications on substrate metabolism has been created.

Post-translational protein modifications include phosphorylation, acetylation, glycation, and O-GlcNAcylation. For phosphorylation, the involvement of the energy sensing kinase, AMP-activated protein kinase (AMPK), has been reviewed by Jason Dyck and colleagues [1] in the context of how AMPK controls cellular metabolism as well as other aspects of overall cellular health and survival. As our understanding of the post-translational regulation of proteins has grown, the involvement of acetylation is also reviewed. The review by Arata Fukushima and Gary D. Lopaschuk [2], details the studies demonstrating how acetylation controls cardiac fatty acid β-oxidation in obesity, diabetes, and heart failure. In addition, the role of acetylation as a control mechanism for transcriptional regulation in the healthy and stressed hearts, is reviewed by Ravi Ramasamy and colleagues [3], providing further evidence of the importance of acetylation in the control of a wide variety of cellular processes.

Adding to this growing list of post-translational protein modifications that regulate protein function are both O-linked attachment of the monosaccharide β-*N*-acetylglucosamine (O-GlcNAcylation) as well as glycation, which involves a complex set of pathways that mediates advanced glycation endproduct (AGE) formation. Luc Bertrand and colleagues [4] discuss the molecular regulation of protein O-GlcNAcylation and describe the role of this process in various cardiac pathologies, whereas Ann Marie Schmidt and colleagues [5] review the recent work in the field highlighting the roles for AGE formation in obesity and atherosclerosis and discuss how new approaches may be used to prevent the adverse consequences of AGEs. Lastly, as multiple post-translational processes can regulate the ability of the cardiomyocyte to transport fatty acids into the cell for subsequent energy production, Joost J Luiken, Jan. F.C. Glatz, and colleagues [6], review the post-translational control of the major protein involved in fatty acid transport, i.e., CD36, and discuss the importance of this regulation on cardiomyocyte function in health and disease.

Another area of research of this special issue is related to protein catabolism and amino acid metabolism. For the former, the importance of autophagy in the turnover of cellular proteins and how this contributes to overall cell health has now been established. Based on this, Traci L Parry and Monte S Willis [7] review the regulation of autophagy by ubiquitin ligases, review the studies that demonstrate how this cellular process can alter cardiac metabolism, and discuss how regulating autophagy may be useful as a therapeutic strategy to protect the heart. For amino acid metabolism, recent evidence has shown that the types of amino acids used by the heart for energy also influences overall cardiac function. Indeed, given the emerging data implicating branched chain amino acid metabolism in a variety of metabolic diseases as well as heart failure, Yibin Wang and Haipeng Sun [8] review how branched chain amino acid metabolism is altered in heart failure and the consequences of these alterations heart failure. P. Christian Schulze and Xiaokan Zhang [9] also review how miRNAs regulate important metabolic pathways in heart failure and discuss the potential benefits of using miRNAs as therapy for heart disease. Lastly, Merry L. Lindsey and colleagues [10] discuss how the inflammatory response in involved in many forms of cardiac pathologies and the need to better understand how macrophages regulate both reparative responses of the left ventricle following myocardial infarction.

Overall, this collection of reviews highlights the importance of cardiovascular metabolism in cardiovascular disease and reviews multiple regulatory circuits that contribute to disease pathogenesis. The focus of this special issue highlights some of the emerging areas of research that provide mechanistic insight into cardiac and vascular metabolic dysregulation. It is anticipated that this collection of reviews will provide insight into new areas of investigation that emphasize the importance of post-translational protein modifications, amino acid metabolism and protein catabolism on substrate metabolism and overall cardiovascular health.

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Dr. Jan F.C. Glatz is currently a Professor of Cardiac Metabolism at the Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, the Netherlands. He studied chemistry and biochemistry (Nijmegen and Utrecht) and received his PhD degree from Nijmegen University in 1983 on the basis of a thesis on fatty acid metabolism in cardiac and skeletal muscle. At present he is also chair of the Department of Genetics & Cell Biology and deputy-chair of the Department of Clinical Genetics (Academic Hospital Maastricht). Dr. Glatz has also served as President of the Society for Heart and Vascular Metabolism from 2012-2015. Dr. Glatz' major contributions to understanding cardiac metabolism include the disclosure of the molecular mechanism of cardiac fatty acid uptake, in particular the role of membrane substrate transporters (e.g., CD36) and of cytoplasmic fatty acid-binding protein, and the unraveling of the role of altered cardiac fatty acid handling in obesity-induced cardiac insulin resistance and diabetic cardiomyopathy. His main current scientific interest is the regulation of energy metabolism in the healthy and diabetic heart with focus on the application of intracellular membrane substrate transporter recycling for so-called metabolic modulation therapy.

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